REMARKS

Status of the Claims

Claims 1-7, 9-21 and 23-33 are currently pending and under consideration. Claims 34-36 have been added. No new matter has been added as a result of these amendments.

Rejection of Claims 1-7, 9-21, and 23-33 Under 35 U.S.C. §103 (a)

The Office Action rejects claims 1-7, 9-21, and 23-33 under 35 U.S.C. §103 (a) as being unpatentable over (a) Phillips (U.S. Pat. No. 6,489,346 B1) (hereinafter "Phillips I"); and (b) Phillips (U.S. Pat. No. 5,840,737) (hereinafter "Phillips II") in view of Phillips I. Applicants respectfully traverse these rejections.

a) Rejection over Phillips I.

The Examiner states that Phillips I teaches a method for treating acid-related gastrointestinal disorders comprising administering to a patient a non-enteric pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent, wherein the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. (See, Office Action, page 4). According to the Examiner, Phillips I teaches that mixtures of the buffering agents can be utilized. The Examiner states that Phillips I discloses as suitable buffering agents the following: sodium bicarbonate, potassium bicarbonate, aluminum hydroxide/sodium bicarbonate co-precipitate and sodium carbonate. The Examiner further states that potassium carbonate is disclosed at column 22, lines 7-8. Additionally, according to the Examiner, sodium bicarbonate is provided in amounts of about 1000 mg to about 1680 mg. The Examiner states that this range is an overlapping range, which meets the instantly claimed range of about 125 mg to about 1000 mg of sodium bicarbonate. The Examiner further states that the non-enteric proton pump inhibitors include a substituted benzimidazole of lansoprazole or salts thereof.

(See, Office Action, page 5). According to the Examiner, Example IV at column 22, lines 1-39 demonstrates an effervescent formulation whereby omeprazole powder was diluted with sodium bicarbonate, citric acid and potassium carbonate to form a homogenous mixture of omeprazole powder. The Examiner concedes that Phillips I does not teach an equimolar ratio of sodium bicarbonate and sodium carbonate. Nevertheless, the Examiner states that prior art teaches the use of the same drug and the same components in similar dosage forms as the instant invention. According to the Examiner, it would have been obvious to one of ordinary skill in the art (hereinafter referred to as a "skilled artisan"), to determine the suitable or effective amounts through the use of routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art. The Examiner states that "absent evidence to the contrary, the instant 'equimolar ratios' as claimed fail to impart any unexpected results." (See, Office Action, page 5). The Examiner claims that the prior art addresses the concern of avoiding large amounts of bicarbonate or other buffers by administering a single dose, which does not require any further administration of a bicarbonate. The Examiner concludes that the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Applicants respectfully traverse this rejection.

Phillips I does not either expressly or inherently teach the equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Similarly, Phillips I does not teach an equimolar ratio of sodium bicarbonate and sodium carbonate. Phillips I discloses a composition comprising a non-enteric coated proton pump inhibitor and at least one buffering agent. With respect to buffering agents, Phillips I states that the preferred buffering agent is sodium bicarbonate. (See, Phillips I, column 13, lines 33-40). Although the reference states broadly that "many other weak and strong bases (and mixtures thereof) can be utilized" and provides a non-exhaustive list of examples of buffering agents including sodium bicarbonate, potassium bicarbonate,

magnesium hydroxide, etc., nowhere does Phillips I suggest an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Phillips I describes more than 32 different buffering agents in addition to various mixtures of these agents. Nothing in Phillips I makes it obvious to a skilled artisan to select an equimolar ratio of specific salts out of all the possible buffer combinations. In fact, Phillips I teaches that a preferred buffering agent is a sodium bicarbonate solution; thus, there is no motivation for a skilled artisan to try to replace the preferred buffering agent with an equimolar ratio of buffering agents as taught in the instant invention.

The Examiner states that

> Applicant's argument that 'Phillips I does not disclose an equimolar ratio of a carbonate salt and a bicarbonate salt as is presently claimed' is not persuasive since Applicants have not demonstrated any superior results attributable to the claimed 'equimolar ratio' amount. The prior art vividly recognizes and teaches similar proton pump inhibiting formulations comprising the incorporation of suitable carriers and buffers to effectively treat acid-related gastrointestinal disorders. (See, Office Action, page 12).

Applicants respectfully disagree. It is known in the art that sodium bicarbonate produces gas while neutralizing stomach acids. In fact, as little as a half teaspoon of sodium bicarbonate liberates as much as 475 mL of carbon dioxide. The formation of this case causes distension of the stomach which results in a bloated feeling, belching and flatulence. (See the enclosed articles "Excessive Gas: What Can Be Done?" from www.uspharmacist.com/oldformat.asp?url=newlook/files/Cons/ACF2FD5.cfm&pub_ and Chapter 15 – Drugs and Gastrointestinal (GI) Disorders from www.pharmacy.utah.edu/pharmtox/common_meds/icm15.html). Also, it is also known in the art that sodium biocarbonate ingestion can cause the spontaneous rupture of the stomach (See, Mastrangelo, M., et al., *Annals of Internal Medicine,* 101(5): 649-650 (November 1984)).

The specification clearly demonstrates superior results attributable to the equimolar ratio of sodium carbonate and sodium bicarbonate (hereinafter referred to as "carbicarb"), namely, the reduction in the comparative amounts of gas, including CO_2 gas, that is produced. This reduction in gas reduces the distension of the stomach, belching and flatulence experienced by patientss who take the compositions of the present invention when compared to patients who take compositions containing solely containing sodium bicarbonate (such as those compositions disclosed in Phillips I and Phillips II). In addition, patients ingesting the compositions of the present invention may have a lower risk of stomach rupture when compared to patients who ingest compositions containing solely sodium biocarbonate.

Applicants draw the Examiner's attention to Example 1 in the specification. In this example, Applicants quantified the gas produced by the neutralization of simulated gastric fluid (hereinafter "SGF") by carbicarb and by sodium bicarbonate *in vitro*. As Applicants demonstrated, there was a fourteen-fold reduction in the volume of the total gas produced, and a two-fold reduction in the volume of CO_2 gas produced in the SGF-carbicarb reaction as compared to the SGF-sodium bicarbonate reaction. (See, specification, page 13, Table 1). Thus, carbicarb is significantly superior to the preferred buffering agent of Phillips I, sodium bicarbonate. Further, as Example 2 demonstrates, less carbicarb is required to neutralize gastric fluid as compared with sodium bicarbonate. (See, specification, pages 13-14, Table 2.)

Thus, Applicants demonstrated that claimed equimolar ratio has an unexpected significant advantage over the prior art buffering agents. As discussed in the *Manuel of Patent Examining Procedure,* Section 2144.05 III (8th Edition, Latest Revision August 2005), citing *In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990):

> The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims....[I]n such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range.

Applicants have demonstrated that the particular range (i.e., an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal) is critical, since the use of this ratio results in an unexpected improvement relative to the prior art range. There is no suggestion anywhere in Phillips I that an equimolar ratio may work better than other possible buffer combinations. It was, therefore, not obvious for a skilled artisan to arrive at the conclusion that the equimolar ratio is indeed important. The situation is therefore analogous to a very broad disclosed genus of substances which does not render *prima facie* obvious specific substances within its scope.

Accordingly, Applicants have satisfied the above discussed test.

b) Rejection over Phillips II in view of Phillips I.

The Examiner states that Phillips II teaches a method for treating gastric acid disorders by administering to a patient a single dose of a pharmaceutical composition including an aqueous solution/suspension of proton pump inhibitors in a pharmaceutically accessible carrier wherein the carrier comprises a bicarbonate salt of a Group IA metal. (See, Office Action, page 6). According to the Examiner, Phillips II also teaches a pharmaceutical composition which includes omeprazole or other substituted benzimidazoles and derivatives thereof in a pharmaceutically acceptable carrier wherein the carrier comprises a bicarbonate salt of a Group IA metal. The Examiner further states that Phillips II teaches a method for treating gastric acid disorders wherein the Group IA metal is sodium and potassium.

According to the Examiner, the pharmaceutically acceptable carrier taught

by Phillips II includes the bicarbonate salt of the Group IA metal and can be prepared by mixing the bicarbonate salt of the Group IA metal, preferably, sodium bicarbonate, with water. The Examiner states that the concentration of the bicarbonate salt generally ranges from approximately 5.0% to about 60.0%. The preferred salt is sodium bicarbonate and its preferred concentration in the solution is about 8.4%. (See, Office Action, page 7).

The Examiner acknowledges that Phillips II does not explicitly teach the equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Similarly, Phillips II does not teach an equimolar ratio of sodium bicarbonate and sodium carbonate. Nevertheless, the Examiner raises the argument which is essentially identical to the Examiner's argument in the §103 (a) rejection over Phillips I, namely, that Applicants have not demonstrated any unusual/unexpected results that accrue from the instant equimolar ratios. (See, Office Action, page 8). According to the Examiner, it is obvious to a skilled artisan to arrive at suitable ratios and/or amounts through routine or manipulative experimentation. The Examiner states that the prior art recognizes that need to administer lower amounts of bicarbonate to avoid adverse effects. The Examiner further acknowledges that Phillips II does not teach a carbonate salt of the Group IA metal. However, the Examiner deems it obvious to a skilled artisan to include the carbonate salt of the Group IA metal of Phillips I with the teachings of Phillips II because Phillips I teaches buffering agents comprising both carbonates and bicarbonates of Group IA metals and teaches that the buffering agents function by elevating the stomach pH to achieve adequate bioavailability of the drug.

Applicants respectfully disagree. As discussed previously herein, Phillips I does not teach the equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. While Phillips I discloses a broad mixture of possible buffering agents, there is no teaching or suggestion to use the equimolar mixture, specifically, carbicarb. Since Applicants demonstrated unexpected and beneficial results stemming from utilizing carbicarb, the invention

is not rendered obvious by Phillips I either by itself or in combination with Phillips II. Phillips II does not cure the deficiency of Phillips I since, as the Examiner acknowledges, Phillips II does not teach a carbonate salt of the Group IA metal at all. On the contrary, Phillips II expressly states that in the preferred embodiment, omeprazole is mixed with a sodium bicarbonate solution to achieve a desired final omeprazole concentration. (See, Phillips II, column 7, lines 64-67). In fact, Phillips II is directed to a method of treating gastrointestinal conditions by administering omeprazole in a carrier with a bicarbonate salt of a Group IA metal, wherein the administration step consists of a single dosage. Moreover, the claims of Phillips II are limited to a carrier **consisting essentially** of a bicarbonate salt of a Group IA metal. (See, Phillips II, column 22, lines 40-48). Therefore, a skilled artisan would not be motivated to replace the bicarbonate salt of a Group IA metal with an equimolar mixture of carbonate and bicarbonate. Phillips II allegedly works for its intended purpose, therefore there is no incentive for a skilled artisan to combine it with Phillips I to achieve the same purpose.

Therefore, contrary to the Examiner's argument, a skilled artisan would not have been motivated to include the carbonate salt of the Group IA metal of Phillips I with the teachings of Phillips II which teaches bicarbonate salts of the Group IA metal, among many other possible buffering agents. Even if one were to combine Phillips I and Phillips II, for which Applicants submit there is no motivation, suggestion or teaching to do so, the resulting formulation would still not comprise an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Neither Phillips I nor Phillips II disclose, suggest or teach such combination; specifically Phillips I teaches a broad mixture of possible buffering agents without any hints of benefits of using the equimolar mixture, and Phillips II teaches only a bicarbonate salt of a Group IA metal without any mentioning of a carbonate salt.

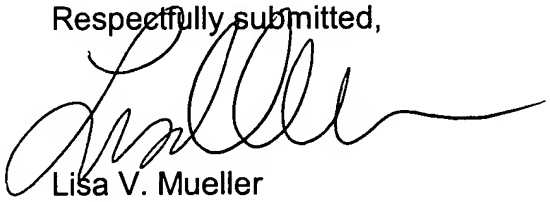
Therefore, Applicants respectfully submit that the rejections of claims 1-7, 9-21, and 23-33 under 35 U.S.C. §103 are improper and should be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Section 103. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,



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August 29, 2006